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The role of ion/neutral complexes in the fragmentation of *N*-benzyl-(alkylpyridinium) ions

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Dedicated to Professor Tino Gäumann on the occasion of his 85th birthday.

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ABSTRACT

N-Benzylpyridinium ions bearing an alkyl group at the pyridine nucleus were studied as potential precursors of gaseous ion/neutral complexes. The occurrence of I/N complexes [$C_6H_5CH_2^+$ ··· alkylpyridine] was probed by the reactivity of the potential benzylic hydride donor sites present in the *ortho*-, *meta*- and *para*-alkyl groups (R = methyl, ethyl, isopropyl and benzyl). Collision-induced dissociation of the ions, carried out in an electrical ion cage mass spectrometer, revealed that hydride transfer strongly depends both on the energy requirements of the hydride transfer but also on the position of the hydride donor. Hydride transfer, giving rise to the loss of toluene, was found to occur exclusively with those *N*-benzylpyridinium ions which bear an isopropyl or a benzyl substituent in the *ortho* position of the pyridine ring, thus reflecting the intermediacy of I/N complexes. All of the putative hydride donor alkyl groups were found to be non-reactive in the *meta* and *para* positions, as were methyl and ethyl groups even in the *ortho* positions. Density functional calculations (B3LYP/6-311+G/3d,2p)//(B3LYP/6-31+G(d)) on the hydride-transfer and simple-cleavage channels were carried out to help rationalizing these observations. The results suggest that the intra-complex hydride abstraction from the 3- and 4-isopropyl- and from the 3- and 4-benzylpyridine neutrals, although being thermodynamically favorable, is suppressed by substantial intra-complex rotational (or reorientation) barriers.

1. Introduction

N-Benzylpyridinium ions are well known in mass spectrometry for their role as suitable species to probe the internal energy deposition on ions generated under various ionization conditions [1–11]. The propensity of such "thermometer ions" to cleanly undergo dissociation of the benzylic C–N bond depends not only on the external conditions of the ion source but, in particular, on the electronic properties of the reactant. Therefore, various electron-releasing and electron-withdrawing substituents have been introduced into the benzylic moiety of the *N*-benzylpyridium ion to affect the energy requirements of the C–N bond cleavage. The readiness to release the corresponding $C_7H_6X^+$ ions, which should mostly retain their (original) benzylic structure but are also believed to partially rearrange by ring expansion to tropylium ions [9,10], provides a suitable indicator for the mildness or roughness of the ionization conditions.

However, gaseous *N*-benzylpyridinium ions could be ideal species to study another important probe reaction, namely, intramolecular hydride transfer. This process has been used extensively to probe the formation of ion/neutral complexes [12–21] as reactive intermediates during mass spectrometric fragmentation [22–30]. As has been shown, a large number of metastable *tert*-butylbenzenium and related $[M+H]^+$ ions eliminate isobutane, necessarily formed via an intra-complex hydride transfer, rather than just releasing the *tert*-$C_4H_9^+$ ion or eliminating isobutene by intra-complex proton transfer. Similar to the *N*-benzylpyridinium ions, even tiny differences in the "electronic" conditions of the reactants strongly affect the relative weight of the hydride transfer process [24,25,27].

Recently, the fragmentation of various di-, tri- and tetrabenzylammonium ions was found to occur predominantly via I/N complexes, reflecting the intra-complex reactivity of benzyl cations towards the aromatic π-systems and benzylic hydride donor sites of the neutral constituent [31]. A very recent paper reported on the substituent effects on the fragmentation of *N*-benzylpiperidinium and *N*-benzylpiperazinium ions bearing various electronically active substituents (X) in the benzylic moiety of the reactants [32]. Again, hydride transfer leading to the loss of the corresponding toluene derivatives was indicative of I/N complexes, such as [X–$C_6H_4CH_2^+$ ···· *c*-$(CH_2)_5NH$], as reactive intermediates during the fragmentation of such relatively simple cyclic ammonium ions.

In view of all these findings, we raised the question whether suitable *N*-benzyl-(alkylpyridinium) ions, bearing alkyl groups as potential hydride donor sites at the heterocyclic moiety, would represent useful model ions for probing the intermediacy of I/N

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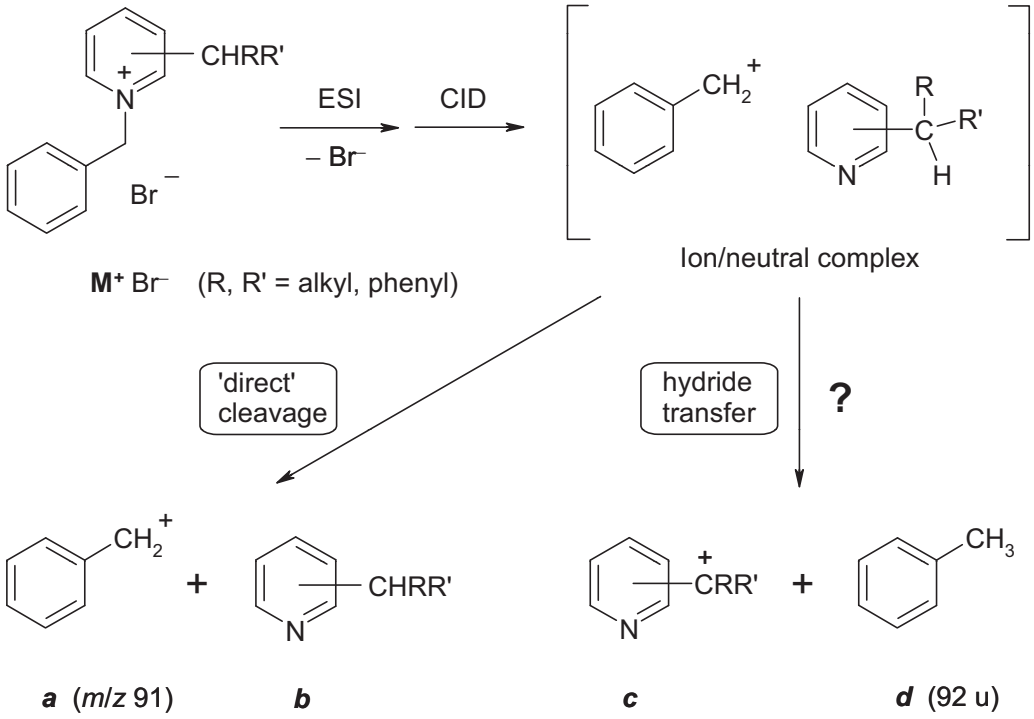


Scheme 1. Fragmentation of *N*-benzyl-(alkylpyridinium) ions, generated by ESI from the corresponding bromides, via two competing channels under ESI/CID conditions:. Benzylic cleavage (left) and rearrangement via an I/N complex (right).

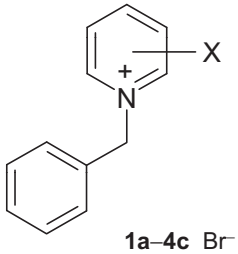
complexes during fragmentation (Scheme 1). To the best of our knowledge, this variant has never been applied to benzylpyridinium thermometer ions. In the present work, we report our results on the fragmentation of a set of *N*-benzyl-(alkylpyridinium) ions ($\mathbf{M^+}$) which, after collisional activation in an ion cage mass spectrometer, should be able to undergo the 'direct' dissociation reaction giving the (parent) $C_7H_7^+$ ions (***a***) and the neutral alkylpyridines ***b*** and, in competition, the elimination reaction generating the corresponding (α-substituted) azabenzylium ions ***c*** and toluene (***d***) by intra-complex hydride transfer. In this case, different from all the previous studies, the electronic properties of the alkyl-substituted pyridine moiety as a leaving group and/or as a hydride donor should govern the course of the fragmentation and, in particular, the role of the putative ion/neutral complexes.

2. Experimental

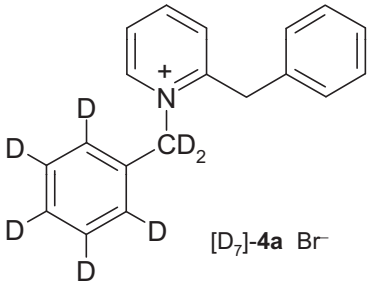
2.1. Compounds

The *N*-benzyl-(alkylpyridinium) bromides (Scheme 2) were synthesised by heating solutions of the appropriate alkylpyridines (10 mmol) (see below) and freshly distilled benzyl bromide (10 mmol) in dichloromethane (15 mL) for 5–6 h. Stirring was continued overnight. The reaction was monitored by TLC and mostly driven to completion. Removal of the solvent under reduced pressure gave crystalline products or viscous oils. These crude products were subjected to the ESI measurements in most cases.

Some of the alkylpyridines were not commercially available. The 2-, 3- and 4-isopropylpyridines were prepared by Grignard reaction of the respective picolinic acid methyl or ethyl esters with methyl magnesium iodide. The resulting pyridyl carbinols were reduced by use of hydroiodic acid and red phosphorous at 150–160 °C [33]. Work-up including kugelrohr distillation (85–90 °C, 7 mbar) gave the corresponding isopropylpyridines in moderate yields (*ortho*, 43%; *meta* 20%; and *para*, 44%) as colorless liquids. 3-Benzylpyridine was synthesized by Wolff–Kishner reduction of 3-benzoylpyridine (675 mg, 3.7 mmol) with hydrazine hydrate (600 μL) and powdered potassium hydroxide (800 mg) in diethylene glycol (10 mL). The mixture was heated to reflux (130 °C) for 5 h and then the temperature was slowly increased to 195 °C and kept for 2.5 h. Work-up gave a crude product (650 mg) and subsequent kugelrohr distillation yielded the product (385 mg, 62%) as a colorless liquid. ^{1}H NMR spectroscopy confirmed the purity of the compound. The *N*-[D_7]benzyl-2-benzylpyridinium



	X		X
1a	2-methyl	**3a**	2-isopropyl
1b	3-methyl	**3b**	3-isopropyl
1c	4-methyl	**3c**	4-isopropyl
2a	2-ethyl	**4a**	2-benzyl
2b	3-ethyl	**4b**	3-benzyl
2c	4-ethyl	**4c**	4-benzyl



Scheme 2. Compounds and ions studied.

Table 1
Relative reaction enthalpies[a,b], ΔH_{diss} and ΔH_{elim}, for fragmentation of selected *N*-benzyl-(alkylpyridinium) ions and relative enthalpies of the I/N complexes and the transition state for the hydride transfer step [/B3LYP/6-311+G(3d,2p)//B3LYP/6-31+G(d)].

Pyridinium ion	Ion/neutral complex ΔH_{INC}	$M^+ \rightarrow a + b$ ΔH_{diss}	TS of H^- transfer ΔH_{TS}	$M^+ \rightarrow c + d$ ΔH_{elim}
1a	158.4	202.4	228.1	252.4
1c	164.1	214.2	258.2	294.6
2a	157.7	201.4	181.6	178.5
2c	164.0	215.9	206.3	227.1
3a	169.7	211.3	173.3	123.2
3c	167.9	219.5	178.0	164.2
4a	n.d.	206.8	n.d.	130.0
4c	n.d.	220.1	n.d.	165.1

[a] Obtained from the total electronic energies (E_{total}) and the standard enthalpies (H°_{298}) relative to those of the respective N-benzyl-(alkylpyridinium) ions.
[b] Given in kJ mol^{-1}.

bromide [D_7]-**4a** Br^- was prepared using perdeutero benzyl bromide prepared from commercially available [D_8]-toluene (Merck, D content >99.5%).

2.2. Mass spectrometric measurements

ESI(+)/CID mass spectra were recorded by use of an Esquire 3000 ion trap (ion cage) mass spectrometer (Bruker Daltonik GmbH, Bremen, Germany) equipped with a standard nanoESI source. Samples were introduced as dichloromethane solutions by self-made nanospray needles. Isolation of the ions prior to CID was done using a small isolation window of about 1 u. Nitrogen, generated by a Bruker nitrogen generator NGM 11, was used as a drying gas. Helium served as a cooling gas for the ion trap and as a collision gas for MS/MS experiments. The spectra shown were recorded with the Bruker Daltonik Esquire NT 5.2 Esquire Control software by accumulating and averaging several single spectra. DataAnalysis™ 3.4 was used for spectra processing.

2.3. Computational methods

All calculations were performed with the *Gaussian 03* package [34] using the hybrid DFT functionals at the level B3LYP/6-311+G(2d,3p//B3LYP/6-31G(d)). Wong and Radom have recommended this procedure as a good compromise between reliability and economy of the computation of large systems [35]. The structures of the *N*-benzylpyridinium ions studied here and carrying the alkyl substituent at the *ortho*- or *para*-position, of their relevant fragmentation products and of the reaction intermediates were optimized using the basis set 6-31+G(d), and harmonic vibrational analysis of the optimized structures were performed at this level. All calculated species have the correct number of imaginary frequencies, i.e., zero for stable ions, molecules and ion-neutral complexes and one for transition states. In the latter case, visualization by the *GaussView* program was used to ensure that the imaginary frequency corresponds to the correct movement of atoms along the respective reaction coordinate. Single point calculations of the optimized structures by B3LYP with the basis set 6-311+G(3d,2p) yielded the total electronic energy, E_{total}, which was converted to the enthalpy H_{298} at 298 K by correction with the zero point energy and the thermal enthalpy correction taken from the harmonic vibrational analysis. The reaction enthalpies ΔH_r relative to the corresponding parent *N*-benzylpyridinium ion, which are presented in Table 1 and which are used in the discussion, were calculated from the values of H_{298}.

It should be mentioned that pre-optimization of the structures by the semi-empirical method AM1 was used to obtain good starting structures for the DFT calculations, which ensured fast convergence of the calculations. However, the optimized structures of transition states and of ion/neutral complexes obtained by AM1 and by B3LYP, turned out to be very different. Further, the B3LYP calculations of the ion/neutral complexes converged very slowly, and at the end of the optimization procedure the calculation oscillated between various similar structures which differed in E_{total} by less than 5 kJ mol^{-1} and were distinguished only by a small rotation of the methyl groups of the substituent.

3. Results and discussion

3.1. Collision-induced dissociation of N-benzyl-(alkylpyridinium) ions

A set of twelve *N*-benzyl-(alkylpyridinium) bromides, **1a** Br^- to **4c** Br^-, and one deuterium-labelled analogue, [D_7]-**4a** Br^- (Scheme 2), were prepared in dichloromethane solutions and subjected to electrospray ionization in an electrical ion cage. The collision-induced dissociation of the corresponding free pyridinium ions was determined under similar conditions and found to be relatively insensitive against variations in the collision potential. As expected, the release of $C_7H_7^+$ ions was found to be ubiquitous and dominant in all cases. In fact, and to some extent surprisingly, all of the methyl- and ethylpyridinium ions **1a**–**1c** and **2a**–**2c** dissociated by exclusive loss of the alkylpyridine neutral; no hydride transfer or any other fragmentation process occurred. Moreover, the same holds true for all of the *N*-benzylpyridinium ions bearing alkyl substitutents of any kind at the *meta* or *para* positions (e.g., **3b**–**3c** and **4b**–**4c**). Again, formation of $C_7H_7^+$ was observed as the only fragmentation pathway. The latter finding was surprising since the benzyl substituent, in particular, on the pyridine ring was expected to provide two amply activated hydride donor C–H bonds.

However, significant elimination of C_7H_8 (most probably as toluene) was found to occur in two cases, viz., the *ortho*-isopropyl- (**3a**) and the *ortho*-benzylpyridinium (**4a**) ions. The contrast between the positional isomers is illustrated for the case of the two isopropyl analogues **3a** and **3c** in Fig. 1, and the corresponding CID spectrum of the *ortho*-benzyl analogue **4a** is shown in Fig. 2. Although the formation of ions [**3a**–C_7H_8]$^+$ and [**4a**–C_7H_8]$^+$ falls far short of that of the $C_7H_7^+$ ions, their relative abundances are in line with expectation: The *ortho*-benzyl substituent represents a slightly better hydride donor than the isopropyl group, as reflected by the ion abundance ratios {[**4a**–C_7H_8]$^+$}:{$C_7H_7^+$} = 0.17 and {[**3a**–C_7H_8]$^+$}:{$C_7H_7^+$} = 0.069. Interestingly, the *ortho*-benzyl analogue **4a** was found to react through a third fragmentation channel, viz. loss of C_6H_6. Benzene elimination is known as a characteristic feature of protonated alkylbenzenes and their derivatives [36–38]; therefore, the observation of ions [**4a**–C_6H_6]$^+$ indicates the formation of substituted benzenium (or arenium ions) [39] as reactive intermediates in the fragmentation of the *ortho*-benzyl-substituted *N*-benzylpyridinium ions **4a**. Since both the loss of toluene and of benzene from ions **4a** should occur via reactive benzyl cations released into ion/neutral complexes (vide infra), the

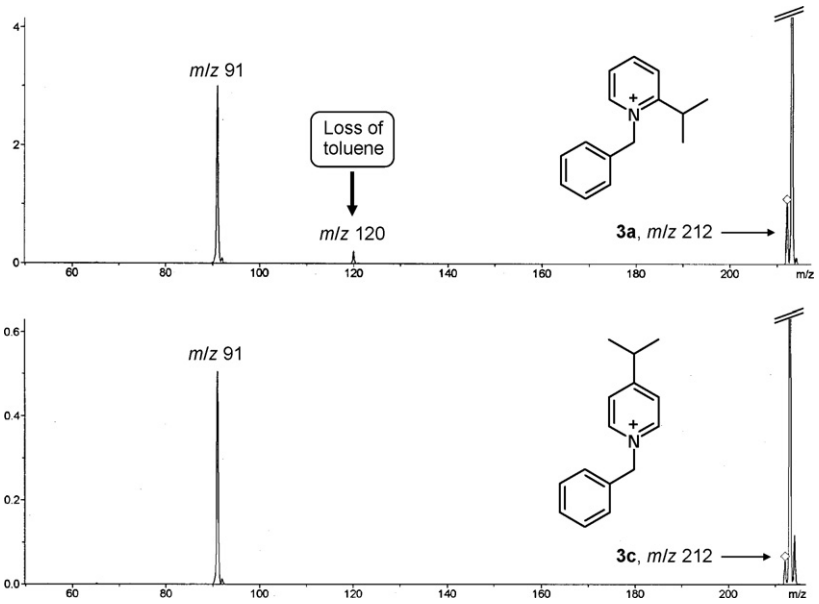


Fig. 1. ESI/CID mass spectra of the 2- and 4-isopropyl-substituted *N*-benzylpyridinium ions **3a** (top) and **3c** (bottom). The signals at *m*/*z* 213 and 214 are due to the mostly non-activated naturally occurring [$^{13}C_1$]-isotopomers.

latter intermediates are crucial to the formation of a relatively large amount of fragment ions relative to that of the "normal" $C_7H_7^+$ ions, ({[**4a**−C_7H_8]$^+$} + {[**4a**−C_6H_6]$^+$}):{$C_7H_7^+$} = 0.48.

3.2. Fragmentation via ion/neutral complexes

We assume that the cleavage of the benzylic C–N bond in all of the *N*-benzylpyridinium ions generates ion/neutral complexes, as insinuated in Scheme 3. As shown above, most of these intermediates are non-reactive in that they simply dissociate without any further intra-complex reaction, giving rise to the exclusive or far predominant formation of $C_7H_7^+$ ions. Only the I/N complexes generated from the *ortho*-isopropyl and the *ortho*-benzyl analogues **3a** and **4a**, respectively, containing neutral alkylpyridine constituents with strongly activated tertiary or benzylic C–H bonds as hydride donors, are able to eliminate toluene. It appears that this specificity reflects the vicinity of the *N*-benzyl group and the hydride-donor methyne or methylene groups, respectively, as a peculiar kind of ortho effect occurring within the ion/molecule complexes. It might be argued that the loss of toluene from **3a** and **4a** involves non-classical transition states instead of non-covalently bound intermediates, a situation which could be envisioned for the *ortho*-substituted species but not in the *meta* and *para* isomers.

In this respect, however, the observation of benzene loss from the benzyl analogue **4a** is particularly telling. This fragmentation necessarily requires the formation of a non-covalently bound intermediate, in which the benzyl cation released from the nitrogen atom can attack the π-system of the other benzyl group to form an *ipso*-protonated diphenylmethane (benzylbenzenium ion **5**, Scheme 3). Such arenium ions are known to undergo both a slow interannular and a fast intraannular proton transfer (proton ring walk) prior to the loss of benzene [36–40]. In the present case, the basic 2-pyridyl group may also interfere in the "proton dance" [41] but it is obvious that one of the mobile protons is transferred to the terminal benzene ring of ion **5**, giving rise to isomer **6** from which benzene is lost eventually. (Note that the related *ring*-protonated tautomers and other tautomeric arenium ions that may be envisioned in this process are not shown in Scheme 3). Admittedly, the structure of the final fragment ion [**4a**−C_6H_6]$^+$ (*m*/*z* 182) depicted in Scheme 3 is tentative. However, this ion is believed to be the

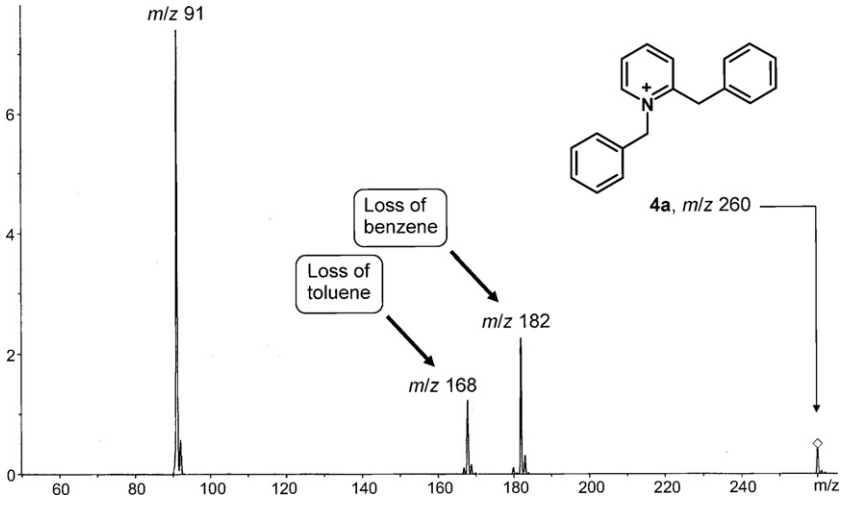
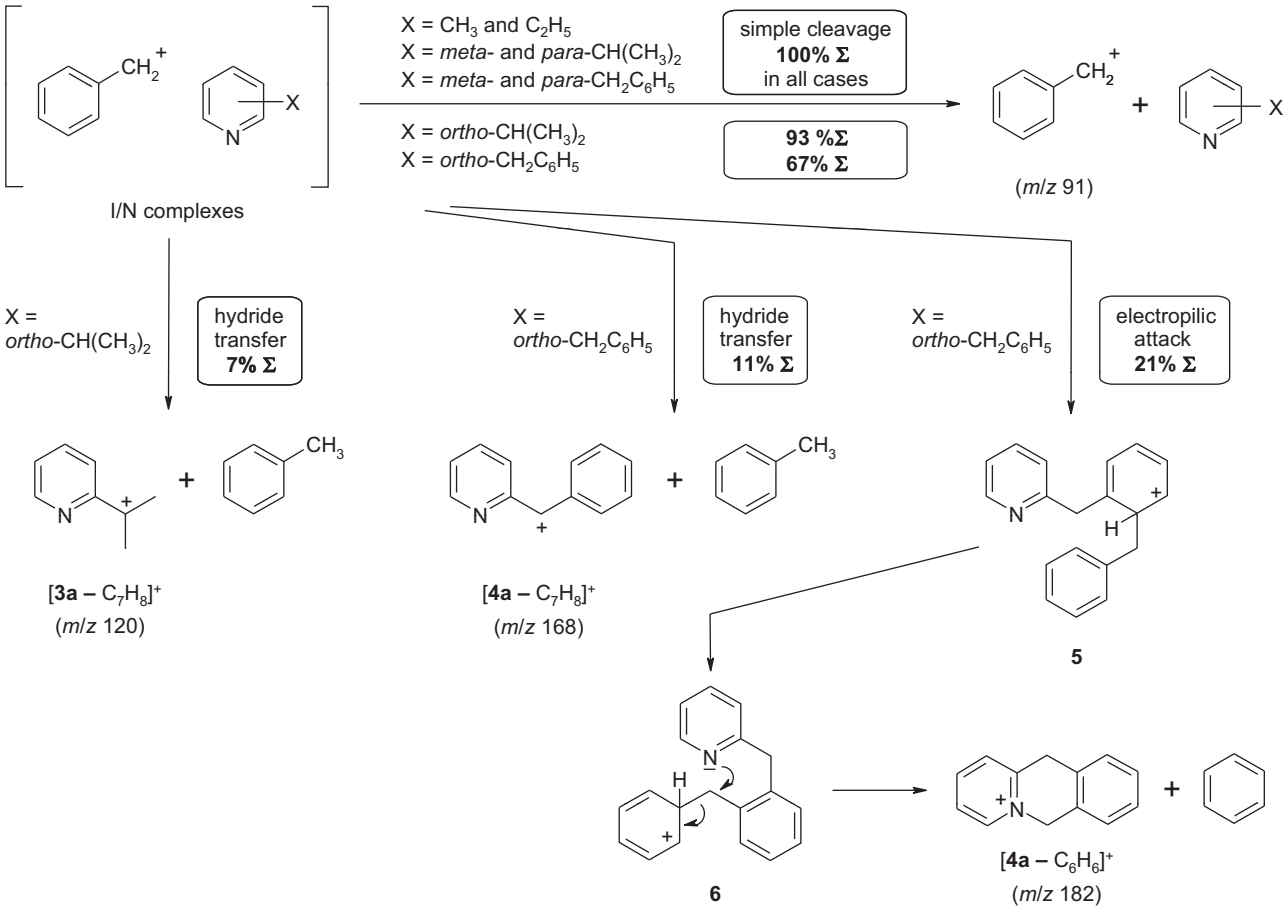


Fig. 2. ESI/CID mass spectrum of the 2-benzyl-substituted *N*-benzylpyridinium ion **4a**.



Scheme 3. Fragmentation of the ion/neutral complexes as both non-reactive and reactive intermediates during the fragmentation of alkyl-substituted *N*-benzylpyridinium ions **1a**–**4c**.

most stable ionic fragment formed by benzene loss from ions **4a** and its formation via ions **5** and **6** necessarily requires an intra-complex electrophilic attack of $C_7H_7^+$ ions at the *ortho*-position of the 2-benzylpyridine constituent.

The mechanism proposed above strongly corroborates the intermediacy of ion/neutral complexes [$C_6H_5CH_2^+$ ··· alkylpyridine] in general, as depicted in Scheme 3. It is confirmed by the fragmentation of the isotopomer [D_7]-**4a**, which contains a fully deuterium-labelled *N*-benzyl and an unlabelled *ortho*-benzyl group (Fig. 3). Besides the expected formation of ions $C_7D_7^+$ (*m*/*z* 98) formed by the direct C–N bond cleavage reaction, loss of [D_7]toluene and [D_5]benzene were observed, giving rise to the ions at *m*/*z* 168 and *m*/*z* 184, respectively. The formation of the latter ions, in particular, reveals that the original *N*-benzylic (dideutero) methylene unit is incorporated into the fragment ion, a typical feature of the intermolecular methyne-group transfer of benzyl cations and related electrophiles ($X–CH_2^+$) to aromatic partners [36–39,42]. Interestingly, a minor amount of the ions undergoes

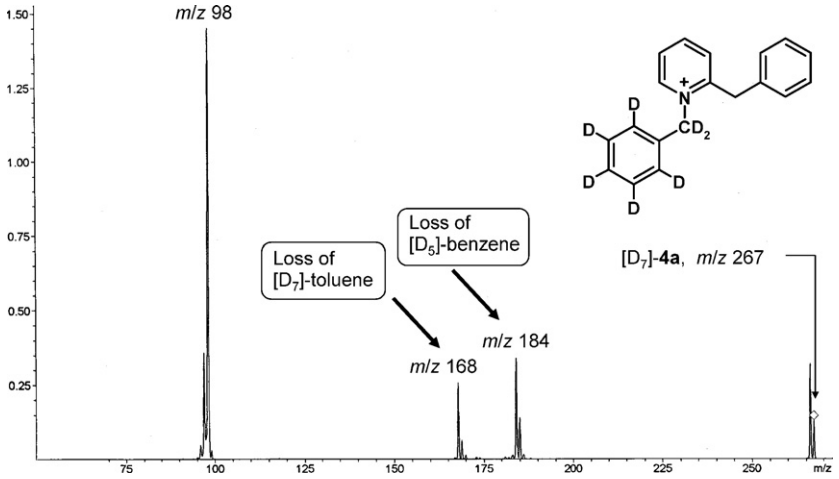


Fig. 3. ESI/CID mass spectrum of the *N*-[D_7]benzyl-2-benzylpyridinium ion [D_7]-**4a**.

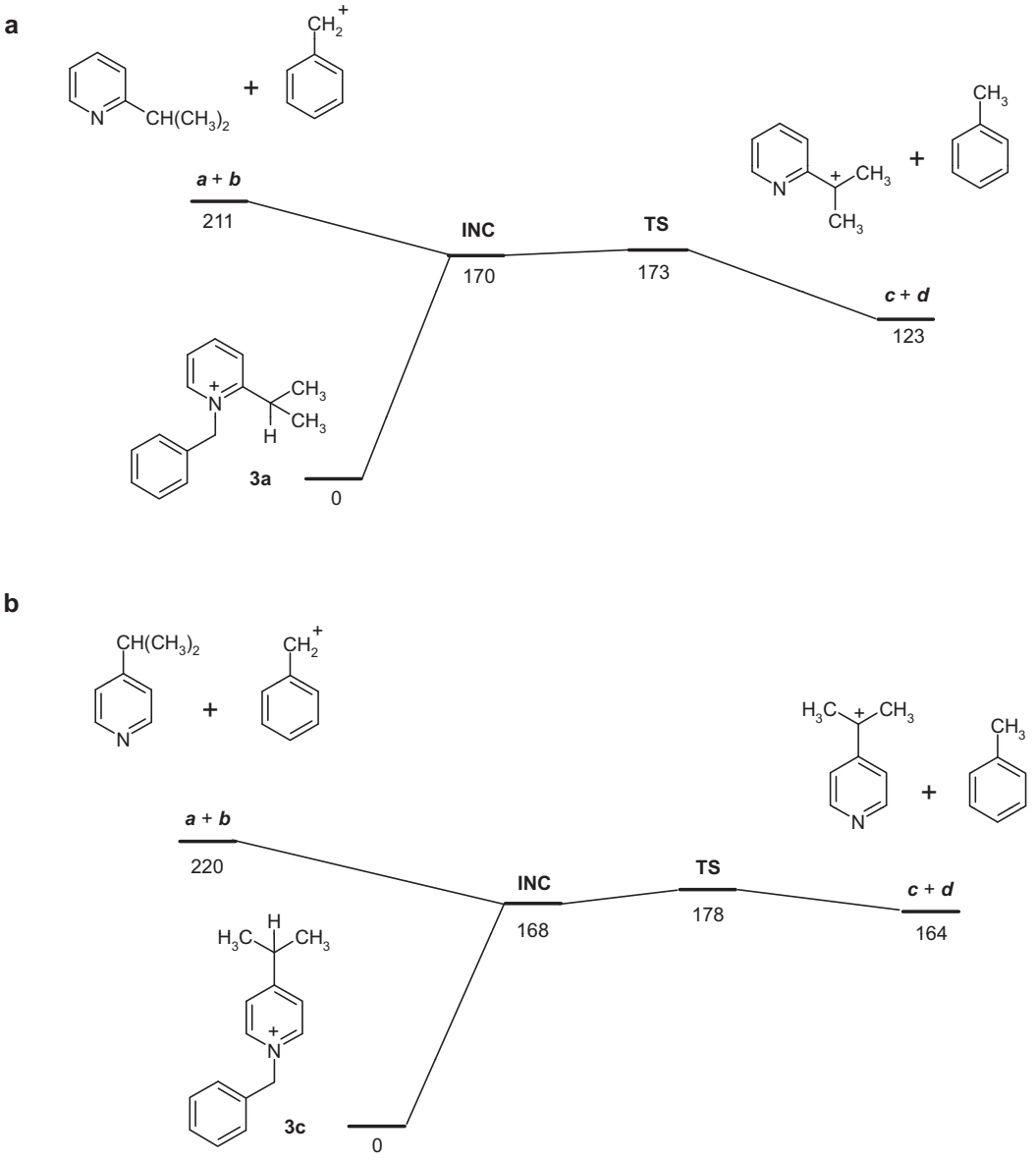


Fig. 4. Energy profiles for the simple C–N bond cleavage (***a*** + ***b***) and the elimination of toluene (***c*** + ***d***) of the *N*-benzyl-(isopropylpyridinium) ions **3a** and **3c**, as calculated by B3LYP/6-311+G(3d,2p)//B3LYP/6-31+G(d) (kJ mol^{-1}).

an intramolecular H/D exchange which, again, is typical for protonated diphenylmethane and its higher homologues [36–38,40,43] and which, on its own, can be used as a structural probe reaction [44]. Finally, the formation of $C_7HD_6^+$ ions (*m*/*z* 97) along with the expected $C_7D_7^+$ ions (*m*/*z* 98) should be noted. Their occurrence points either to the reversibility of the whole isomerization process (with the fraction of $C_7HD_6^+$ being eventually released from the pyridine N atom) or to a competing protonolytic cleavage of the diphenylmethane moiety in the intermediate ion **5**. Notably, the occurrence of the ions $C_7HD_6^+$ should *not* be considered a hint to the ring expansion of the benzyl cations released from the "thermometer ions" discussed in the literature [9,10].

3.3. Computational results

To shed some more light on the fragmentation of the *N*-benzyl-(alkylpyridinium) ions, we calculated the energy requirements for direct dissociation giving the benzyl cation and the alkylpyridine and for the hydride transfer reaction yielding toluene and an azabenzyl cation for the *ortho*-isomers **1a**–**4a** and the *para*-isomers **1c**–**4c**. The data relevant for the present discussion are collected in Table 1 as enthalpy differences ΔH°_{298} comparing the combined products of fragmentation, the I/N complexes and the transition states for the hydride transfer relative to the enthalpies of the parent *N*-benzyl-(alkylpyridinium) cations. (On request, the full details of the calculations can be obtained from the authors.) The energy requirements for the dissociation does not depend on the nature of the alkyl substituent ($\Delta H_{diss} = 206 \pm 5$ kJ mol^{-1} was calculated for the *ortho*-substituted ions and $\Delta H_{diss} = 217 \pm 3$ kJ mol^{-1} for the *para*-substituted congeners). In all cases, the I/N complexes were found to be more stable than the dissociation products (***a*** + ***b***) by $\Delta H_{diss} - \Delta H_{INC} = 46 \pm 5$ kJ mol^{-1}.

By contrast to the dissociation reaction, the reaction enthalpy computed for the elimination of toluene decreases from $\Delta H_{elim} = 252$ kJ mol^{-1} for the *ortho*-methyl derivative **1a** to $\Delta H_{elim} = 123$ kJ mol^{-1} and $\Delta H_{elim} = 130$ kJ mol^{-1} for the *ortho*-isopropyl and *ortho*-benzyl congeners, **3a** and **4a**, respectively. Clearly, "localized bond activation", a long-established concept in organic mass spectrometry [45–47], strongly affects this reaction channel, as presumed. As a consequence, fragmentation via the

hydride transfer route is energetically more favorable than the direct dissociation in the case of the *ortho*-ethyl derivative **2a**, both of the isopropyl derivatives **3a** and **3c**, and also for both of the benzyl derivatives **4a** and **4c**. In fact, the decomposition of the I/N complexes, which is always endothermic for the direct dissociation channel, becomes exothermic for the toluene loss from both of the isopropyl-substituted ions **3a** ($\Delta H_{elim} - \Delta H_{INC} = -47$ kcal mol^{-1}) and **3c** ($\Delta H_{elim} - \Delta H_{INC} = -4$ kcal mol^{-1}), as illustrated in Fig. 4. Very likely, this holds also true for the benzyl-substituted ions **4a** and **4c**. However, while the direct dissociation of the I/N complexes does not require any additional activation exceeding the reaction enthalpy, the hydride transfer within the I/N complex is expected to proceed over an activation barrier. We were able to locate transition states for this process; their enthalpies, ΔH_{TS}, relative to the parent *N*-benzyl-(alkylpyridinium) ions are also collected in Table 1. In the case of ions **1a**, **1c** and **2c**, for which the elimination of toluene is calculated to be thermodynamically unfavorable, considerable activation enthalpies, $\Delta H_{TS} - \Delta H_{INC}$, relative to the I/N complexes were obtained (ca. 70, 94 and 42 kJ mol^{-1}, respectively). The corresponding structures represent transition states, in which the transfer of the migrating hydride and formation of the toluene molecule is almost complete. By contrast, in the case of the remaining parent ions **2a**, **3a** and **3c**, the activation barriers for hydride transfer within the I/N complexes are quite small (ca. 24, 4 and 10 kJ mol^{-1}, respectively) and the transition states exhibit the expected "normal" structures. Since the activation enthalpies of the hydride transfer are small and elimination of toluene is energetically more favorable than the direct dissociation of the I/N complexes, the computational results suggest that the toluene elimination route should be observable for the *N*-benzyl-(alkylpyridine) ions **2a** and **3a**–**3c**, and likely for all of the *N*-benzyl-(benzylpyridinium) isomers **4a**–**4c** as well.

Nonetheless, the experiments show that toluene elimination is only significant for the *ortho*-substituted ions **3a** and **4a**. This contrast between the experimental and computational results discussed so far is striking. Obviously, an additional effect is operating which hinders the hydride transfer within the I/N complexes of the *meta*- and *para*-isomers even if this route is energetically significantly more favorable than the direct dissociation of the I/N complexes. We suggest that this is an entropic effect which is due to fact that direct dissociation of the I/N complexes is possible for all conformations and all mutual orientations of the two components, the benzyl cation and the alkylpyridine, within the I/N complex, while the hydride transfer requires a specific relative orientation of the components to proceed towards the transition state. Closer inspection of the optimized structures of the I/N complexes shows that all these structures are similar and exhibit a rather tight aggregation of the benzyl cation to the nitrogen atom of the neutral alkylpyridine by two hydrogen bonds between an H atom of the methylene group and an H atom at the *ortho*-position of the benzyl cation. This is shown in Fig. 5 for the I/N complexes arising from the two isopropyl-substituted ions **3a** and **3c**. In the case of the *ortho*-isomer **3a**, the benzyl cation is situated in the neighborhood of the isopropyl group and the changeover to the transition state of the hydride transfer requires only a small shift of the benzyl cation. Obviously, this is a very favorable case for the successful competition of the toluene elimination with the direct dissociation of the I/N complex. At variance from the *ortho*-isomer **3a**, the hydride transfer within the I/N complex formed from the *para*-isopropyl isomer **3c** requires a complete reorientation of its components to achieve the transition state structure, which obviously cannot compete with its direct dissociation. In general, it is postulated that the ionic component of an I/N complex is free to change its orientation and to move over quite large molecular distances. However, this may be an oversimplification in particular for I/N complexes

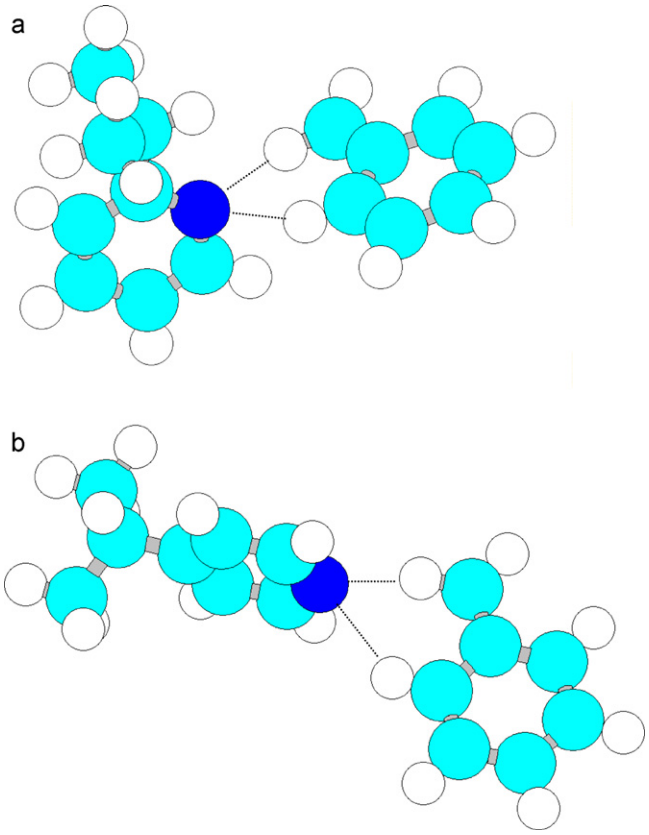


Fig. 5. Minimum structures of the ion/neutral complexes generated from (a) the *N*-benzyl-(*ortho*-isopropylpyridinium) ion **3a** and (b) the *N*-benzyl-(*para*-isopropylpyridinium) ion **3c**, as calculated by B3LYP/6-311+G(3d,2p)//B3LYP/6-31+G(d). The dashed lines indicate the shortest atomic distances between the constituents of the I/N complexes.

such as those studied here. In fact, the benzyl cation is of similar size as the neutral component, the alkylpyridine, and the positive charge is well delocalized. The separation from the N atom, being the negative end of the dipolar alkylpyridine, may allow the bulky benzyl cation to leave the sphere where electrostatic attraction keeps the components of the I/N complex together; as a consequence, the complex dissociates instead of adopting a reoriented constellation that would allow the hydride transfer to occur. Obviously, this scenario occurs for the I/N-complexes of both the *meta*- and the *para*-somers.

As mentioned above, it can be argued that the loss of toluene from the energetically suitable *ortho*-alkylpyridinium ions may take place by a concerted process and not involve a reactive I/N complexes at all. This would mean that the *meta*- and *para*-isomers do not eliminate toluene because such concerted processes are mechanistically impossible in these cases. However, the finding that the *ortho*-benzyl analogue **4a** also fragments by elimination of benzene necessarily requires the interplay of a non-covalently bound intermediate, as shown in Scheme 3. Of course, the electrophilic attack of the $C_6H_5CH_2^+$ ion, after its release from the pyridine nitrogen atom, at the *ortho*-benzyl group may also happen within a relatively tight aggregate, and reorientation of its constituents to a more loosely bound I/N complex is intercepted by the subsequent rearrangement steps [48]. On the whole, however, and in view of their thermodynamic stability as compared to the simple C–N bond cleavage, it appears that ion/neutral complexes of the general form [$C_6H_5CH_2^+ \cdots$ alkylpyridine] are involved in the fragmentation of the *N*-benzyl-(alkylpyridinium) ions investigated here.

4. Conclusion

N-Benzylpyridinium ions bearing a tertiary alkyl or a benzyl group at the *ortho*-position of the pyridine nucleus eliminate toluene by hydride transfer from the α-C–H donor site of that *ortho* substituent. Our ESI/CID measurements indicate that this elimination pathway can compete with the simple C–N bond dissociation releasing the $C_7H_7^+$ ions because of local C–H bond activation at the hydride donor site. However, the very same bond activation does not assist the elimination of toluene from the isomeric *meta*- and *para*-alkyl-substituted *N*-benzylpyridinium ions. Therefore, it appears that the constituents of the ion/neutral complexes [$C_6H_5CH_2^+$ ··· alkylpyridine] generated from the reactive *ortho*-isomers can adopt an intra-complex orientation enabling the hydride transfer, whereas a suitable reorientation cannot be adopted in the I/N complexes formed during the fragmentation of the *meta*- and *para*-isomers [49]. The intermediacy of I/N complexes is also supported by the loss of benzene originating from the *N*-benzyl group of the *N*,2-dibenzylpyridinium ions **4a**. Further studies should shed more light onto the surprising *ortho* specificity of the toluene elimination from the isomeric *N*-benzyl-(alkylpyridinium) ions.

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